

## AMENDMENTS

### Amendments to the Claims:

The following listing of claims will replace all previous listings and versions thereof:

42. (Currently amended): A method for selecting a compound which reduces the activity of [[a]]an SCN1A sodium ion channel comprising:

- (a) contacting a composition comprising a recombinantly expressed human alpha subunit of an SCN1A sodium ion channel protein;
- (b) assaying the activity of the human alpha subunit of the SCN1A sodium ion channel in the presence of said test compound;
- (c) comparing the activity of the human alpha subunit of the SCN1A sodium ion channel in the absence of said test compound; and
- (d) selecting a compound which reduces the activity of the human alpha subunit of the SCN1A sodium ion channel as compared to the activity of the SCN1A sodium ion channel in the absence of the test compound,

wherein said human alpha subunit of the SCN1A sodium ion channel protein is selected from the group consisting of:

- (i) SEQ ID NO:3;
- (ii) SEQ ID NO:4;
- (iii) [[an]] a human SCN1A protein having a sodium channel activity and encoded by ~~an-the~~ SCN1A nucleic acid sequence ~~having at least 95% identity to the nucleic acid set forth in SEQ ID NO:1 or 2;~~
- (iv) ~~the a human~~ SCN1A protein of (iii) comprising a mutation corresponding to amino acid position 188 of SEQ ID NO:3 which replaces an aspartic acid residue by a valine residue and encoded by an SCN1A nucleic acid sequence having at least 95% identity to the nucleic acid set forth in SEQ ID NO:1 or 2;

- (v) ~~the a human~~ SCN1A protein of ~~(iii)~~ comprising a mutation corresponding to amino acid 1238 of SEQ ID NO:3 which replaces a glutamic acid residue by an aspartic acid residue and encoded by an SCN1A nucleic acid sequence having at least 95% identity to the nucleic acid set forth in SEQ ID NO:1 or 2; and
- (vi) ~~the a human~~ SCN1A protein of ~~(iii)~~ comprising a mutation corresponding to amino acid position 1773 of SEQ ID NO:3 which replaces a serine residue by a tyrosine residue and encoded by an SCN1A nucleic acid sequence having at least 95% identity to the nucleic acid set forth in SEQ ID NO:1 or 2.
43. (Previously presented): The method of claim 42, wherein said method is used for selecting a compound capable of reducing voltage-gated ion channel activity of a human SCN1A protein associated with idiopathic generalized epilepsy (IGE).
44. (Previously presented): The method of claim 42, wherein said method is used for selecting a compound capable of reducing voltage-gated ion channel activity of a human SCN1A protein associated with generalized epilepsy with febrile seizures.
45. (Previously presented): The method of claim 42, wherein said test compound is comprised in a library of test compounds.
46. (Currently amended): The method of claim 42, wherein [[a]]an SCN1A nucleic acid encoding said SCN1A protein is comprised in an expression vector.
47. (Previously presented): The method of claim 46, wherein said expression vector is comprised in a cell.

48. (Previously presented): The method of claim 42, wherein said assaying is performed in a cell free system.
49. (Previously presented): The method of claim 42, wherein said assaying is performed with a whole cell.
50. (Previously presented): The method of claim 42, wherein said ion channel activity is:
- (i) voltage dependence activation;
  - (ii) voltage dependence of steady state level of inactivation;
  - (iii) time course of inactivation;
  - (iv) the number or fraction of channels available for opening;
  - (v) change in current;
  - (vi) flux of ions through the channel;
  - (vii) phosphorylation of channel;
  - (viii) binding of molecules to the channel; or
  - (ix) induction of a cellular messenger.
51. (Previously presented): The method of claim 50, wherein said flux of ions through the channel is assessed by:
- (i) fluorescence resonance energy transfer (FRET)-based voltage sensor assay;
  - (ii) dibasic dyes;
  - (iii)  $^{14}\text{C}$ -guanidine;
  - (iv) two electrode voltage clamp; or
  - (v) patch-clamp.
52. (Previously presented): The method of claim 50, wherein said binding of molecules to the channel is assessed by surface plasmon resonance.
53. (Currently amended): The method of claim 42, wherein said method is used for selecting a compound which reduces the hyperexcitability state of [[a]]an SCN1A ion channel.

54. (Currently amended): The method of claim 42, wherein SEQ ID NO:3 is obtained from [[a]]an SCN1A nucleic acid sequence encoding SEQ ID NO:3.
55. (Currently amended): The method of claim 42, wherein SEQ ID NO:4 is obtained from [[a]]an SCN1A nucleic acid sequence encoding SEQ ID NO:4.
- 56.-59. (Canceled)
60. (Previously presented): The method of claim 47, wherein said cell is an indicator cell.
61. (Currently amended): The method of claim 42, wherein said alpha subunit of the SCN1A sodium ion channel is the SCN1A protein of (iii) ~~having at least 95% identity to the amino acid sequence set forth in SEQ ID NO: 3.~~
62. (Currently amended): The method of claim [[61]]42, wherein said alpha subunit of the SCN1A sodium ion channel is the SCN1A protein of (iv) comprises comprising a mutation at amino acid position 188 of SEQ ID NO:3 which replaces an aspartic acid residue by a valine residue and encoded by an SCN1A nucleic acid sequence having at least 95% identity to the nucleic acid set forth in SEQ ID NO:1 or 2.
63. (Currently amended): The method of claim [[61]]42, wherein said alpha subunit of the SCN1A sodium ion channel comprises a mutation at amino acid 1238 of SEQ ID NO:3 which replaces a glutamic acid residue by an aspartic acid residue.
64. (Currently amended) The method claim [[61]]42, wherein said alpha subunit of the SCN1A sodium ion channel comprises a mutation at amino acid position 1773 of SEQ ID NO:3 which replaces a serine residue by a tyrosine residue.
65. (New): The method of claim 62, wherein said alpha subunit of the SCN1A sodium ion channel is the SCN1A protein of (iv) comprising a mutation at amino acid position 188 of

SEQ ID NO:3 which replaces an aspartic acid residue by a valine residue and encoded by an SCN1A nucleic acid sequence set forth in SEQ ID NO:1 or 2.